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Supplementary appendix

This appendix formed part of the original submission. We post it as supplied by the authors.

This online publication has been corrected. The corrected version first appeared at thelancet.com on November 8, 2021.

Supplement to: Grange Z, Buelo A, Sullivan C, et al. Characteristics and risk of COVID-19-related death in fully vaccinated people in Scotland. *Lancet* 2021; published online Oct 28. http://dx.doi.org/10.1016/S0140-6736(21)02316-3.

Supplementary Material

Contributors: AS, CR, ZG and JM conceived this study. AB, CS, ZG, EM, UA, CMC, AS and CR commented on the paper, oversaw the analysis and edited the final manuscript. AB, CS, ZG EM, UA, CMC, CR and AS led the writing of the paper. AB, KB and EM accessed and verified the underlying data and were responsible for data cleaning and analysis. All the authors contributed to the study design. All the authors contributed to drafting the paper and revised the manuscript for important intellectual content. All the authors gave final approval of the version to be published.

S1: Methods

Data from all individuals from Scotland from several national datasets, including Electronic Communication of Surveillance in Scotland (ECOSS), National Clinical Datastore (NCDS), Rapid Preliminary Inpatient Data (RAPID), Scottish Intensive Care Society Audit Group (SICSAG) and National Records of Scotland (NRS), were linked using the Community Health Index (CHI) numbers. Of nearly 8 million vaccination records, only ~0.01% did not have a valid CHI number. Information on comorbidities were extracted and linked from the EAVE-II cohort, which is a national surveillance platform established to report on the epidemiology of COVID-19. The number of individuals who received each vaccine type was extracted from the public-facing Public Health Scotland Daily Dashboard. 214 individuals received two different vaccines; given the extremely small proportion of individuals receiving mixed-doses compared to single-vaccine types, this was not incorporated into further analysis.

Survival analysis – death rate per 10,000 person-years.

Confirmed COVID-19 death rates were calculated for individuals who were unvaccinated and fully vaccinated, stratified by age group. Where an individual died due to COVID-19, their vaccination status was determined at time of their positive reverse-transcription polymerase chain reaction (RT-PCR) test. Person-years were calculated from time the first individual became fully vaccinated (December 29, 2020), up to and including the final day at which a confirmed COVID-19 death was recorded (August 18, 2021).

The population used in this analysis was taken from the vaccine patient analysis database, which contained patient level data on all individuals eligible for vaccination in Scotland. At the time of this analysis, individuals

under the age of 16 were not eligible for vaccination, with the exception of those deemed 'clinically extremely vulnerable'. Due to this, there were little to no data on children and young people; they were therefore not considered in this analysis unless they turned 16 during the study period. Such individuals were entered into the study on the day of their 16th birthday. Using data from the death register, individuals who died prior to December 29, 2020 were excluded; those who died during the study period i.e. December 29, 2020 to August 18, 2021 were censored on their date of death. Person-years were counted from time spent by individuals in relevant age-bands. Where individuals had transitioned between vaccination status and age-bands during the study period, they were censored and re-entered into the study in their new relevant cohort.

Cox Proportional Hazards Model. Cox regression was used to model the hazard ratio (HR) for a COVID-19 death following a positive test in fully vaccinated individuals, accounting for age, sex, number of comorbidities and deprivation quintile. Age and time were included as spline terms. Risk groups were according to QCOVID risk groups (https://qcovid.org/) and were referred to as comorbidities in the main text for ease of understanding.[1] All individuals ≥14 days post second vaccine dose with a positive test within the study time-period were included in the model. The outcome of interest was time from positive test to death from COVID-19 (as confirmed by death certificate). Individuals were censored at the study end date or if they died within the study period of non-COVID-19 causes on the date of death.

Persons were modelled separately according to whether the test result was from a Lighthouse test (community testing) or NHS test lab (testing on admission to hospital). Those tested in the community were likely to be less unwell than those first tested on admission to hospital. Those not tested before admission were likely either be persons with serious symptoms of COVID-19 who did not realise that COVID-19 was a possible cause of their illness or urgent/emergency admissions to hospital for other causes who incidentally test positive. Initial modelling confirmed that those tested in NHS labs were >10x more likely to die of COVID-19 than those tested in the Lighthouse lab. We have reported primarily on the findings from the Lighthouse lab results as these numbers were more representative of the Scottish population than those testing positive in NHS labs.

There were three individuals in our dataset where "COVID-19, virus not identified" or U07.2 code was listed as their underlying cause of death, whereas 192 individuals had their underlying causes of death listed as "COVID-19, virus identified". All had positive test results. We assumed that for the "COVID-19, virus not identified" categorisation, the medical professional who listed cause of death was unaware that the individual had a positive test already (https://www.who.int/classifications/icd/COVID-19-coding-icd10.pdf), given that our definition of post-vaccination death required a positive RT-PCR test prior to death.

Table S1: ICD-10 codes for COVID-19 illness

Code	Description
U07.1	COVID-19, virus identified
U07.2	COVID-19, virus not identified
Source: https://www.who.int/classifications/icd/COVID-19-coding-icd10.pdf	

S2: Additional Results

There was a median of 69 days (IQR 52 to 86) between an individual being fully vaccinated and subsequently having a RT-PCR positive associated death, which was longer than the median of 47 days (IQR 24 to 77 days) between vaccination and testing positive for post-second dose infected individuals who did not die. As the IQRs substantially overlapped and there were a multitude of variables that could influence the length of time between vaccination and testing positive, such as community transmission rates at the time of infection, health-seeking behaviour, testing availability and so on, considerable caution is needed in interpretation of these findings.

Table S2: Death rates per 10,000 person-years for fully vaccinated and unvaccinated individuals in Scotland stratified by age group, December 29, 2020 to August 18, 2021.

Group	Deaths	Person-Years	Deaths Per 10,000 Person-Years (95% CI)
Ages 18-64			
Fully Vaccinated	30	376,847	0.80 (0.54 – 1.14)
Unvaccinated	472	1,526,010	3.09 (2.82 – 3.39)
Ages 65-79			
Fully Vaccinated	88	211,189	4.17 (3.34 – 5.13)
Unvaccinated	1,015	156,728	64.76 (60.84 – 68.87)
Ages 80+			
Fully Vaccinated	118	84,343	13.99 (11.58 – 16.75)
Unvaccinated	1,597	38,013	420.12 (399.77 – 441.24)

Table S3: Breakdown of risk groups listed in GP records for individuals who died post-second vaccine dose

Risk group	Number
Atrial fibrillation	41
Asthma	20
Blood cancer	11
Heart failure	27
Coronary heart disease	67
Congenital heart disease	7
COPD	48
Dementia	28
Diabetes type 1	1
Diabetes type 2	64
Epilepsy	6
Fracture	27
Neurological disorder	6
Parkinson's	6
Pulmonary hypertension	7
Pulmonary rare	8
Peripheral vascular disease	15
Rheumatoid arthritis or SLE	9
Respiratory cancer	8
Severe mental illness	35
Sickle cell disease	0
Stroke/TIA	47
Thrombosis or pulmonary embolus	26
Chronic kidney disease (3-5)	66

Table S4: Characteristics of individuals who died post-second vaccine dose

Characteristics	Level	Number
Place of test	Lighthouse lab	53
	NHS labs	181
Sex	Female	90
	Male	146
Deprivation status: Scottish Index of Multiple Deprivation (SIMD) 2020	1 – Most deprived	57
	2	57
	3	45
	4	33
	5 – Least deprived	44
Number of risk groups	0	28
	1	37
	2	45
	3-4	81
	≥5	34

Supplementary References:

1. Clift AK, Coupland CA, Keogh RH, Diaz-Ordaz K, Williamson E, Harrison EM, Hayward A, Hemingway H, Horby P, Mehta N, Benger J. Living risk prediction algorithm (QCOVID) for risk of hospital admission and mortality from coronavirus 19 in adults: national derivation and validation cohort study. *BMJ*. 2020; m**3731**.